Remarks

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims and the following remarks.

The Office Action is final. Upon entry of the present Amendment, claims 1-6 and 12-24 are pending in the present application. Claims 7-11 have been cancelled without prejudice. Claims 3, 6 and 13 have been withdrawn from further consideration as being directed to a non-elected invention. Claims 1 and 12 have been amended to further clarify and define the invention. Claim 1 has been amended to incorporate the subject matter of claims 7 and 11, now cancelled.

Entry of the Amendment is proper under 37 C.F.R. § 1.116, since the amendments and remarks are made in response to arguments raised in the final rejection, and place the application in condition for allowance.

Entry of the present Amendment is respectfully requested.

Rejection Under 35 U.S.C § 103(a)

Claims 1, 2, 4, 5, 7-12 and 14-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Patel *et al.*, U.S. Patent Application Publication No. 2005/0181052 (hereinafter "Patel") in view of Scott *et al.*, U.S. Patent No. 6,887,307 (hereinafter "Scott").

Applicants have cancelled claims 7-11, thus rendering moot the rejection as to these claims.

Applicants respectfully traverse the above rejection as applied to the remaining claims.

The Examiner asserts that the present application is obvious in light of the above references, as indicated on pages 3-4 of the outstanding Office Action.

Based on the following, Applicants contend that the Examiner's position is not supportable, and that the presently claimed invention is therefore unobvious over Patel in view of Scott.

The presently claimed invention is directed to a capsule preparation that comprises a capsule shell and contained inside the capsule shell is a medicine unstable to moisture. The medicine unstable to moisture is lansoprazole or an optically active isomer thereof or a salt thereof. The capsule shell is stable in a low moisture state and has pH-independent disintegration properties, and also provided is that the capsule shell excludes hard gelatin and/or hydroxypropyl methyl cellulose as a main component of the capsule shell.

As indicated in MPEP § 2143, the Examiner must resolve the factors described in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which provides the controlling framework for an obviousness analysis, before utilizing the rationales that were established in *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Differences between the Invention and the Cited References

Applicants provide the following information regarding the *Graham* factor of ascertaining the differences between the prior art and the claims that are at issue.

Concerning the Scott reference, Scott states that the advantages of pullulan capsules are "Higher product quality consistency…Relatively low water content…High stability of various properties over storage…." (see Scott, column 3, line 66, to column 4, line 9).

However, the Scott reference does not describe any medicine other than acetaminophen. Further, Scott describes that acid substances are comprised in the capsule (see Scott, claim 4, and column 5, lines 5-12).

Particularly, Applicants note that the Scott reference describes "Especially preferred is ethylenediaminetetraacetic acid or salts thereof or citric acid or salts thereof."

In view of the above, the Patel reference discloses a composition comprising lansoprazole. However, lansoprazole is known to be unstable to acids.

The Cited References Teach Away from the Presently Claimed Invention

Applicants herein enclose for the Examiner's consideration an exhibit, He *et al.*, "*Influences of Sodium Carbonate on Physicochemical Properties of Lansoprazole in Designed Multiple Coating Pellets,*" AAPS PharmSciTech, Vol. 11, No.3, pp.1287-1293 (September 2010).

Specifically, Applicants note paragraphs 2 and 3 from the introduction section (see He *et al.*, page 1287, right column):

> *The PPIs are either imidazopyridine derivatives or substituted pyridylmethylsulfinyl benzimidazole such as…lansoprazole (LSP)…etc. An important physicochemical characteristic of PPIs is the instability to heat, light, and acidic media due to their structural features….LSP…seems to be especially sensitive to such attack compared to the other members of PPIs….Therefore, LSP needs to be protected from the destructive effects of gastric acid when administered orally…..LSP belongs to class II drug, which is characterized by low solubility and high permeability. Moreover, it degrades rapidly in acidic conditions and is stable in basic environment….*

Applicants submit that in view of the enclosed exhibit and the above remarks, the aspects of the Scott reference teach away from the combination of the Scott and Patel references.

"When the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be nonobvious." See MPEP § 2143, and *KSR Int'l Co. v Teleflex Inc.*, 82 USPQ2d 1385, (U.S. 2007).

Since the Scott disclosures teach away from the presently claimed invention, its combination with Patel was improper.

According to the USTPO guidelines, "[i]t is improper to combine references where the references teach away from their combination." See MPEP § 2145, citing *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); see also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354

(Fed.Cir. 2001) ("[A]s a "useful general rule,"...references that teach away cannot serve to create a prima facie case of obviousness." (citations omitted).

No Motivation to Combine the Cited References

For the reasons discussed above, Applicants respectfully submit that there is no motivation for combining the Scott reference (where a capsule comprises acidic substances) with Patel, which relates to a composition comprising lansoprazole (which is unstable to acids).

The intended purpose of the invention disclosed in the Patel reference is to provide a pharmaceutical composition comprising microtablets, wherein said microtablets comprise lansoprazole.... (See Patel, Abstract, and page 1, paragraphs [0010] and [0012]).

Applicants submit that based on the teachings within Scott and the supplied exhibit, the Scott references would render the Patel prior art invention being modified unsatisfactory for its intended purpose.

The USPTO has made it clear that "[i]f [the] proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." See MPEP § 2143.01 V, citing *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984).

Additionally, MPEP § 2143.01 VI plainly states: "The proposed modification cannot change the principle of operation of a reference. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious." See also *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Here, in light of the enclosed exhibit, the proposed combination of the Patel and Scott references would render the Patel invention unsatisfactory for its intended purpose to "provide a pharmaceutical composition comprising microtablets, wherein said microtablets comprise

lansoprazole...." Applicants respectfully submit that this proposed modification of exposure of lansoprazole to acidic substances within a capsule (as indicated in Scott) would radically change the principle of operation of the Patel reference since lansoprazole is known to be unstable to acids.

Therefore, based on the above discussion, Applicants respectfully submit that impermissible hindsight reconstruction was used in support of the rationale relied upon by the Examiner. See MPEP § 2142.

Applicants respectfully submit a *prima facie* case of obviousness cannot be based on the combination of Scott and Patel references.

Applicants submit that based on the differences discussed above, the Examiner has not resolved the *Graham* factor of ascertaining the differences between the prior art and the claims that are at issue, and therefore the rationales the Examiner provides for the rejection are improper.

Applicants note that although the above comments discuss the Scott and Patel references individually, this was only for discussing these references in terms of the *Graham* factor analysis. Applicants submit that taking the above *Graham* analysis in mind, Patel in view of Scott does not lead to the presently claimed invention.

In light of the above amended claims and remarks, Applicants submit that the assertions made by the Examiner regarding the Scott and Patel references are incorrect, thus failing to support the Examiner's position. Accordingly, based on the differences between the presently claimed invention and the above references, the cited references do not teach or suggest the presently claimed invention.

Since amended claim 1 is not obvious to one of ordinary skill in the art, claims 2, 4, 5, 12 and 14-24, which ultimately depend from claim 1, are unobvious over the cited references for the same reasoning discussed above.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Conclusion

Applicants respectfully submit that the rejection raised by the Examiner has been overcome, and that the present application now stands in condition for allowance.

Should there be any outstanding matters that need to be resolved, the Examiner is respectfully requested to contact Paul D. Pyla at the telephone number below, in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized to charge payment or credit any overpayment to Deposit Account No. 23-0975 for any additional fees required under 37 C.F.R. §§1.16 or 1.17.

Respectfully submitted,

Naoki NAGAHARA et al.

By /Paul D. Pyla/ Digitally signed by /Paul D. Pyla/ DN: cn=/Paul D. Pyla/, o, ou, email=ppylaclwenderoth.com, c=US Date: 2011.02.02 14:58:49 -05'00'

Paul D. Pyla
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Attorney for Applicants

Attachment: Exhibit: He *et al.*, "*Influences of Sodium Carbonate on Physicochemical Properties of Lansoprazole in Designed Multiple Coating Pellets,*" AAPS PharmSciTech, Vol. 11, No.3, pp.1287-1293 (September 2010).

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